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Long- and Short-Term Exposure to $PM_{2.5}$ and Mortality:

Using Novel Exposure Models

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Abstract

Background—Many studies have reported associations between ambient particulate matter (PM) and adverse health effects, focused on either short-term (acute) or long-term (chronic) PM exposures. For chronic effects, the studied cohorts have rarely been representative of the population. We present a novel exposure model combining satellite aerosol optical depth and land-use data to investigate both the long- and short-term effects of $PM_{2.5}$ exposures on population mortality in Massachusetts, United States, for the years 2000–2008.

Methods—All deaths were geocoded. We performed two separate analyses: a time-series analysis (for short-term exposure) where counts in each geographic grid cell were regressed against cell-specific short-term $PM_{2.5}$ exposure, temperature, socioeconomic data, lung cancer rates (as a surrogate for smoking), and a spline of time (to control for season and trends). In addition, for long-term exposure, we performed a relative incidence analysis using two long-term exposure metrics: regional 10 × 10 km $PM_{2.5}$ predictions and local deviations from the cell average based on land use within 50 m of the residence. We tested whether these predicted the proportion of deaths from PM-related causes (cardiovascular and respiratory diseases).

Results—For short-term exposure, we found that for every 10-μg/m^3 increase in $PM_{2.5}$ exposure there was a 2.8% increase in PM-related mortality (95% confidence interval [CI] = 2.0–3.5). For the long-term exposure at the grid cell level, we found an odds ratio (OR) for every 10-μg/m^3 increase in long-term $PM_{2.5}$ exposure of 1.6 (CI = 1.5–1.8) for particle-related diseases. Local $PM_{2.5}$ had an OR of 1.4 (CI = 1.3– 1.5), which was independent of and additive to the grid cell effect.

Conclusions—We have developed a novel $PM_{2.5}$ exposure model based on remote sensing data to assess both short- and long-term human exposures. Our approach allows us to gain spatial resolution in acute effects and an assessment of long-term effects in the entire population rather than a selective sample from urban locations.

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Multiple studies in the United States and worldwide have shown associations between exposure to ambient particulate matter (PM) and adverse health effects.[1–6] These adverse health effects include asthma,[7] cardiovascular problems,[3,8–12] respiratory infections,[13–17] lung cancer, and mortality.[18–22]

Previous studies have generally focused on either long-term (chronic) PM exposure[23–26] or short-term (acute) PM exposure.[15,27,28] In addition, studies of acute effects typically depend on $PM_{2.5}$ monitors within their study domain. Because $PM_{2.5}$ concentrations vary spatially within the study domain, this introduces exposure error and likely produces a combination of downward bias in the effect estimates and wider confidence intervals (CIs) due to a mixture of classical and Berkson error.[29] The relative magnitude of the two effects is not yet clear.

The lack of spatially resolved daily $PM_{2.5}$ concentration data restricts most studies to areas surrounding monitoring sites, mostly in cities, which may not be representative of the population as a whole. Such studies have used mostly city-level contrasts, although more recent studies have incorporated estimates from land-use regression. For example, cohort studies with few exceptions (eg, the Six City Study) rely upon convenience samples that are not representative of the population either in demographic or geographic characteristics, raising questions about generalizability and the possibility of selection bias. Suburban, exurban, rural, and semirural populations are particularly under-represented. Similarly, in many studies, minorities and people with lower educational attainment are under-represented. In addition, although land-use regression can produce estimates of exposure at participants addresses, the lack of monitoring in rural areas to calibrate these models has led to the exclusion of participants in such locations even when in the cohort.[24]

Various studies have tried to address this issue. There are some population-based chronic-exposure studies that have assessed within-city exposure and mortality. Naess et al[30] looked at chronic exposure to NO_2, PM_{10}, and $PM_{2.5}$ in 470 neighborhoods and all-cause and cause-specific mortality in Oslo, Norway. Exposures were consistently associated with all causes of death in both age groups for men and women. The associations were particularly strong for chronic obstructive pulmonary disease, which appeared linear whereas cardiovascular causes and lung cancer seemed to have threshold effects. Gan et al[31] looked at specific traffic-related air pollutants associated with coronary heart disease (CHD) morbidity and mortality in Metropolitan Vancouver. This population-based cohort study included a 5-year exposure period and a 4-year follow-up period. Individual exposures to traffic-related air pollutants including black carbon, $PM_{2.5}$, NO_2, and nitric oxide were estimated at residences of the subjects using land-use regression models. An interquartile range elevation in the average concentration of black carbon was associated with a 6% increase in CHD mortality (95% CI = 3–9%) after adjusting for age, sex, preexisting comorbidity, neighborhood socioeconomic status, and copollutants ($PM_{2.5}$ and NO_2). Few studies on the long-term effect of exposure have looked at broader populations. Crouse et al[32] looked at the risk of cardiovascular mortality in relation to long-term exposure and $PM_{2.5}$ in Canada. They assigned estimates of exposure to ambient $PM_{2.5}$ derived from satellite observations to a cohort of 2.1 million Canadian adults. They used both standard Cox proportional survival models and nested, spatial random-effects survival models. For

the Cox models, they showed hazard ratios (HRs) of 1.15 (95% CI = 1.13–1.16) from nonaccidental causes and 1.31 (95% CI = 1.27–1.35) from ischemic heart disease for each 10-μg/m^3 increase in concentrations of $PM_{2.5}$. Using spatial random-effects models controlling for the same variables, they showed HRs of 1.10 (95% CI = 1.05–1.15) and 1.30 (95% CI = 1.18–1.43), respectively.

Other studies have used new methodological approaches in air pollution studies regarding short- and long-term exposure. Künzli[33] presents several key approaches in studies of ambient air pollution. He discusses among other issues how cross-city longitudinal data are needed to estimate both short- and long-term effects, and how time-series studies have previously neglected the long-term component. They also show the importance of disentangling the contributions of different time domains of air pollution exposure. Künzli shows that by considering the geography of susceptibility and exposure, and by using more sophisticated approaches to acknowledge the "geographies of time," studies on the total health effects of ambient air pollution could be considerably improved. Burnett and colleagues[34] showed that results from time-series studies are equivalent to estimates obtained from a dynamic population in which each person's mortality risk can be summarized as the daily number of deaths. The authors showed that the association between temporal variation in the environmental covariates and the survival experience of members of the dynamic population can be estimated by regressing the daily number of deaths on the daily value of the environmental covariates, as is done in time-series mortality studies.

We recently presented a novel method of assessing temporally and spatially resolved $PM_{2.5}$ exposures for epidemiological studies using satellite aerosol optical depth measurements, which makes it possible to predict daily $PM_{2.5}$ concentration levels at a 10 × 10 km spatial resolution.[35] In this previous work, we examined the relationship between $PM_{2.5}$ ground measurements and Moderate Resolution Imaging Spectroradiometer Satellite–derived aerosol optical depth measurements in New England during the period of 2000–2008. Using multistage prediction models, we initially performed day-specific calibrations of the satellite using ground $PM_{2.5}$ measurements from all monitoring sites in New England and incorporating land-use regression and meteorologic variables. This use of daily calibration allows us to get considerably better predictive power, and hence lower exposure error. Later, spatial smoothing was used to predict $PM_{2.5}$ concentrations for grid cell-day combinations when satellite measures are not available. Because our models produced daily $PM_{2.5}$ predictions, not monthly or yearly, this allowed us to estimate the health effects of both short-term and long-term exposures. In addition, the availability of satellite measurements in every grid cell improved spatial predictions, compared with land-use regression models calibrated with monitors in a limited number of locations. Finally, we incorporated land-use regression as a final component, which estimates the difference between neighborhood level (grid cell) values and address-specific $PM_{2.5}$ based on land-use terms within 50 m of the residential address, allowing us to estimate long-term exposure at an address-specific level.

In this follow-up article, we use our model predictions to study the association between both long- and short-term $PM_{2.5}$ exposure and mortality in the entire population of Massachusetts during the period 2000–2008.

METHODS

Study Domain

The study was conducted in Massachusetts (Figure). To avoid boundary effects, some $PM_{2.5}$ data from neighboring states were included in the analysis.

Exposure Data

Data for both short- and long-term $PM_{2.5}$ exposures for the years 2000–2008 were assessed using recently developed prediction models.[35] The Massachusetts exposure dataset encompasses daily $PM_{2.5}$ predictions at a resolution of 10 × 10 km. In addition, we predicted 365-day moving averages of grid-cell $PM_{2.5}$ to look at chronic effects and local deviations from the grid-cell predictions (from land-use regression) on a 50 × 50 m spatial resolution across the state (Figure) during the entire study period. Because the Boston metropolitan area within the Route 128 comprises 15 cells, this allows us to resolve exposure within the city. The local land-use component allows further resolution to the address level, but only for long-term exposure. For more detailed information on the prediction model please refer to Kloog et al.[35] We then generated daily and long-term $PM_{2.5}$ exposure to each decedent based on their address.

Our generated predictions have multiple advantages over other approaches commonly used in other health studies such as inverse distance weighting, kriging, etc. First, the smooth function of latitude and longitude is effectively a weighting scheme, with some important differences. The weights do not have to be isotropic, they can have a functional form be other than inverse distance squared, and they can vary every 2 months (unlike distance-based weights, which are fixed). To this we add the additional information provided by the daily satellite measurement near the residence and the local land-use regression results. There are many US cities with only one monitor close to the city. In such cases, inverse distance weighting would be of no practical use, whereas our methods would produce exposure contrasts across the various cities' 10 × 10 km grid, as well as the local land-use regression.

Mortality Data

Individual georeferenced mortality records were obtained from the Massachusetts Department of Public Health for all available years (2000–2008). The dataset included 468,570 deaths. Our model can include locations both proximate and far from ambient monitoring stations. We defined "near" as within 20 km of an ambient monitor. The near areas contain 80% of the population, with the rest in the "far" areas (more than 20 km from an ambient monitor). Public health records included residential location, place of death, age, sex, date of death, ethnicity, education, and primary cause of death. From these data, we constructed daily death counts for each 10 × 10 km grid cell for our time-series analysis; long-term exposure was assigned based on residential address.

Mortality Covariates

Temperature Data—As in other PM mortality studies, temperature was used as a covariate.[36,37] Temperature data were obtained from the national climatic data center.[38]

Only continuously operating stations with daily data from 2000 to 2008 were used. Grid cells were matched to the closest weather station.

Socioeconomic Data—Socioeconomic variables for the tract level were obtained from the 2000 US census with data on social, economic, and housing characteristics.[39] Socioeconomic variables at the census-tract level included percent minorities, age, education, and income. In addition we used individual socioeconomic variables from the Massachusetts Department of Public Health mortality records (race, education, and sex).

Smoking Surrogate—As a surrogate for cell-specific smoking experience, we used the long-term average lung cancer mortality rate in each cell as a control variable. Lung cancer data were obtained through the Massachusetts Department of Public Health.

Statistical Methods

Geocoded mortality data were matched with our exposure estimates. Because the mortality datasets did not include changes of residence, we had to assume when looking at long-term exposure that the decedents had lived at their current address for several years. This introduces some exposure misclassification. However, we think the misclassification is relatively minor. The average age of decedents in our study population was 75 years, and in the northeast United States, people above the age of 75 have limited mobility (only 2% of the population changed residence during 2009–2010).[40]

We assessed the acute effects of exposure to $PM_{2.5}$ by assigning to decedents the grid exposure (on the day of death and preceding 3 days) corresponding to their residence for deaths outside of hospital. Deaths in hospital may have occurred outside the grid cell of residence, and so for those deaths, we assigned the mean predicted $PM_{2.5}$ concentration in all grid cells within 30 km of the residence, again for the day of death and up to 3 preceding days. Most time-series studies have reported the strongest acute associations with mean $PM_{2.5}$ for the current and previous day, rather than same day exposure[41] or longer lags. We therefore took current and previous day exposures as our primary analysis. As a sensitivity analysis, we also examined $PM_{2.5}$ exposure 2 days before death (lag2) and $PM_{2.5}$ exposure 3 days before death (lag3). Specifically, we modeled the mortality rate λ_{it} in the *i*th cell on the *t*th day as follows:

$$\log(\lambda_{it}) = \alpha + \lambda_i + \beta_1 PM_{it} + \lambda(t) + \text{temporal covariates}$$

where

$$\lambda_i = \delta + \text{spatial covariates} + e_i$$

where PM_{it} is the daily $PM_{2.5}$ concentration in cell i, $\lambda(t)$ is a smooth function of time, temporal covariates are temperature and day of the week, spatial covariates are socioeconomic factors and a surrogate for long-term smoking history, and e_i is the remaining unexplained difference in mortality rate between cell i and other cells (treated as a

mean zero normal random effect with variance estimated from the data). This model expands the usual time-series analysis by including spatial covariates and random intercepts for small areas.

The specific covariates we used were a linear and quadratic term for temperature with the same moving average as $PM_{2.5}$, age, percent minorities, median income, percent of people without high school education, and lung cancer rate as a surrogate for long-term smoking history. $\lambda(t)$ was estimated with a natural cubic spline with 45 degrees of freedom (5 df per year). We used an interaction term between in-hospital death and short-term exposure, to test whether location modified the association.

Long-term exposure was analyzed through a relative incidence analysis. We defined particle-related deaths as those from cardiovascular and respiratory diseases and contrasted those with mortality unrelated to air pollution (accidental death, cancer [except lung cancer], homicide, etc.). Specifically we fit the following model:

$$\text{Logit}(PrMort_{ij}=1|X)=(\alpha+u_j)+\beta_1 PM_{it}+\beta_2 PML_i+\beta_{3i}X_{3i}+\beta_{4i}X_{41}+\ldots(u_j)\sim N[0,\sigma_u{}^2]$$

where $Mort_{ij}$ is the response (particle-related or nonrelated death) for the *i*th subject in grid *j*, α and u_j are the fixed and random (grid-specific) intercepts, respectively, PM_{it} is 365- day moving average ending on day *t*, PML_i is the local (50 m) deviation of $PM_{2.5}$ from the long-term grid-cell average, X_{3i}, etc. denote the set of covariates of interest used in the model, and $\sigma_u{}^2$ is the variance of the random effects.

We also looked at various interactions of interest, including interactions between near and far areas and both short-term and long-term exposure as well as interactions between low and high education groups (based on individual college education) and long-term $PM_{2.5}$ exposure. We considered whether effect estimates differed between the two main cause-specific mortality rates by performing a logistic analysis of cardiovascular and respiratory mortality.

RESULTS

Of the 468,570 deaths included in our analyses, 46% were men, 94% were white, and 20% had higher than a high school education. The average age at death was 75 years (Table 1).

Table 2 summarizes of the exposure and temperature variables used in the analysis. Various lags were tested in the time-series analysis, with the strongest based on the mean of lag01. The results for lag01 are presented as commonly reported in many previous studies.[14,24] For every10-μg/ m^3 increase in short-term $PM_{2.5}$ exposure, there was a 2.8% increase in mortality (95% CI = 2.0–3.5). There was also a significant interaction between short-term pollution and near and far locations ($P < 0.001$). For every10-μg/m^3 increase in short-term $PM_{2.5}$ exposure in the “far” group, there was a 1.4% increase in mortality (95% CI = 0.8–2.0%). For every10-μg/ m^3 increase in short-term $PM_{2.5}$ exposure in the “near” group, there was a 4.5% increase in mortality (95% CI = 2.6–6.5%).

Table 3 presents the odds ratios (ORs) for cardiovascular and respiratory mortality for a 10-$\mu g/m^3$ increase in long-term grid-cell $PM_{2.5}$ exposure for the full datasets and various interactions. The OR was 1.6 (CI = 1.5–1.8) for cardiovascular and respiratory mortality relative to deaths from other causes. Local $PM_{2.5}$ had an OR of 1.4 (CI = 1.3–1.5) in the same model. Because local $PM_{2.5}$ was constructed as the address-specific deviation from the grid-cell average, these effects are independent and additive. There was a significant interaction between education group and long-term pollution ($P<0.001$). The OR for the high education group (college education) was 1.4 (CI = 1.2–1.6), whereas for the remainder the OR was 1.9 (CI = 1.6–2.1). There was also a significant interaction between long-term pollution and near and far groups ($P < 0.001$). The OR for subjects living more than 20 km from a monitor was 1.3 (CI = 1.1–1.6), whereas for those living closer, the OR was 1.7 (CI = 1.5–1.9). The OR for nonwhites (OR 2.9, CI = 1.9–4.5) was higher than for whites (OR 1.6, CI = 1.4–1.7).

The logistic regression comparing cardiovascular and respiratory mortality showed no appreciable differences both for the regional $PM_{2.5}$ and local $PM_{2.5}$ exposure. Similarly, there were no important risk differences between people who died in the hospital and those who died at home.

DISCUSSION

The main feature of this study is the use of novel hybrid prediction models that examine short- and long-term exposure associations with mortality, and include the entire population of the state. Unlike traditional land-use regressions, this model produces daily predictions. This model also performs better in regions far from monitors because the satellite data provide exposure data. In addition, these models can 1) control for small area socioeconomic status variables in time-series analysis and look for effect modification by the same variables; 2) test whether the $PM_{2.5}$ slope is different in people residing far from monitors; 3) assess chronic effects of particles using the entire population, again including people distant from monitors; 4) estimate effects of local traffic–derived particles independent of regional particles; and 5) reduce exposure error and hence downward bias in slopes, and upward bias in CIs. Key findings include differences in the slopes of acute and chronic $PM_{2.5}$ between locations closer or more distant from monitoring stations, interactions of chronic exposure with race and socioeconomic status (with less advantaged groups having stronger associations), and an additional effect of traffic particles generated near the address of the decedents. The Six City Study[42,43] found that a 1-year period for chronic exposure captured essentially the entire effect. Hence our use of a 1-year average should be sufficient to capture the long-term effect of $PM_{2.5}$ exposure.

It is instructive to compare these results with results of previous time-series and cohort studies. Zanobetti and colleagues studied the acute effect of fine and coarse particulate air pollution on mortality in a national analysis of 112 cities. [44] For cities similar to cities in our study (the northeast area, grouped as cities with warm summer-continental), a 10-$\mu g/m^3$ increase in $PM_{2.5}$ was associated with a 1.19% increase (95% CI = 0.73–1.64) in total mortality. A key difference is that they assigned the same daily exposure to all people in each city, whereas we were able to assign different exposures to people on a relatively small

grid. Another key difference is that they analyzed only cities, whereas we could analyze an entire state. Our study finds larger and more precise effect-size estimates despite analyzing fewer deaths, possibly due to reduced exposure error.

Berkson measurement error for exposure would be expected to bias standard errors upward, but not bias effect sizes down, whereas classical exposure error would do the opposite. If exposure error was a mixture of these two types, reduced exposure error could produce results such as we observed. This does not preclude other explanations.

Miller et al[45] reported a relative risk of 1.76 for cardiovascular deaths per 10 μg/m^3 using within-city exposure, and Puett and colleagues[24] used exposure from a land-use regression analysis to estimate a hazard ratio of 1.26 for all-cause mortality (95% CI = 1.02–1.54) with each 10-μg/m^3 increase in annual $PM_{2.5}$ exposure. These estimates are similar to ours and higher than in older studies that did not have geographically resolved exposure. That suggests the exposure error in cohort studies is predominantly classical. The similarly larger estimate in our study supports this conclusion, and also extends the results to suburban and rural residents. Furthermore, our use of satellite exposure data allowed a much larger sample size, with more deaths than in the American Cancer Society (ACS) study, the Nurses' Health Study, and the Six City Study combined. We confirm the results of the ACS study that people with less education have greater susceptibility to particles, although the association in the college educated is still substantial, and with a relatively narrow CI.

Although covariate control is a limitation of this analysis, the use of fine-scale geographically resolved exposure is a clear advantage over studies such as the first reports from ACS study, which used metropolitan areas often encompassing multiple counties, and often with only one monitor available to assign exposure. A reanalysis of the data by Willis et al,[46] restricted to people who live closer to the monitor, reported a doubling of the estimate slope per unit exposure, suggesting substantial downward bias by classical measurement error. These results plus the similarity between our estimates and other estimates based on geographically resolved exposure[24,47] provides some assurance about the generalizability of those estimates. As noted above, we see smaller effects in locations more than 20 km from monitors, which generally have lower population density. This may reflect different composition (more traffic particles in the more densely populated regions), although further analysis is needed to confirm this. Consistent with this, we found that deviations from grid-cell-average $PM_{2.5}$ predicted by land-use terms within 50 m of residence had additional predictive power for mortality. This also suggests that traffic particles are more toxic.

A key difference between our analysis and the ACS or Nurses Health study is that they oversampled the highly educated, undersampled minorities. In general, cohort studies of the long-term effects of $PM_{2.5}$ have been nonrepresentative. Our finding of a substantially stronger associations in nonwhites and the less educated raises an important environmental justice concern.

Another major limitation of the present study is the spatial resolution of 10 × 10 km. We compensate for this in our analysis of chronic effects by using a land-use regression to

compute a local PM variable. Better resolution of the satellite data would clearly be beneficial and should become available. As satellite remote sensing evolves, higher spatial resolution data (eg, 3 × 3 km and 1 × 1 km) will further reduce exposure error. Our mortality datasets did not include changes in residence, which will introduce some exposure misclassification into our study.

In conclusion, our novel prediction models, making use of satellite data on air pollution, perform well in assessing short-term and long-term effects of $PM_{2.5}$ exposure. This enables us to examine entire populations, including exurban and rural locations, with better spatial resolution and tighter CIs for the time-series estimates. The larger effect-size estimates seen in recent cohort studies (using geographically resolved chronic exposures) are supported in this analysis for a whole population. This modeling approach presents new opportunities to study the effects of both short- and long-term particle exposures on human health.

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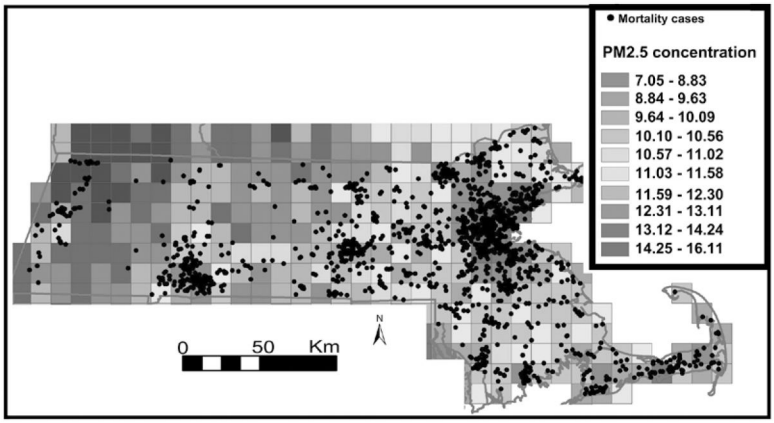

FIGURE.

Map of the study area showing the dithered residential location of a subset of mortality cases over a sample $PM_{2.5}$ ($\mu g/m^3$) 10 × 10 km pollution grid for a sample day (01/07/2001).

TABLE 1

Descriptive Statistics: Deaths in Eastern Massachusetts, 2000–2008

Characteristic	No. (%)
Sex	
Men	216,717 (46)
Women	251,852 (54)
Race	
White	438,402 (94)
Black	17,479 (4)
Other	12,689 (3)
Education (years)	
0–12	372,848 (80)
>12	95,722 (20)
Age (mean years)	75.0

TABLE 2

Descriptive Statistics for $PM_{2.5}$ Exposure and Temperature for 2,495 Days with Available Data, Massachusetts, 2000–2008

	Mean	Median	Standard Deviation	Range	Q1	Q3
Acute PM ($\mu g/m^3$)	9.8	8.7	4.5	93.7	6.6	11.9
Chronic PM ($\mu g/m^3$)	9.9	10.0	1.2	24.1	9.1	10.7
Temperature (°C)	45.6	46.9	19.0	110.3	31.2	62.1

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TABLE 3

ORs for Cardiovascular Disease and Respiratory Mortality for Every10 μg/m^3 Increase in Long-Term $PM_{2.5}$ Exposure

$PM_{2.5}$ Exposure Type	**Odds Ratio (95% CI)**
All mortality cases long-term $PM_{2.5}$	1.6 (1.5–1.8)
All mortality cases local $PM_{2.5}$	1.4 (1.3–1.5)
Urban areas	1.7 (1.5–1.9)
Rural areas	1.3 (1.1–1.6)
High education	1.4 (1.2–1.6)
Low education	1.9 (1.60–2.1)